Pediatric Acute-Onset Neuropsychiatric Syndrome (PANS) as a Post-Infectious Autoimmune Disease: Benefits of Intravenous Immunoglobulin (IVIG)

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Study Sponsor: octapharma

For the safe and optimal use of human proteins

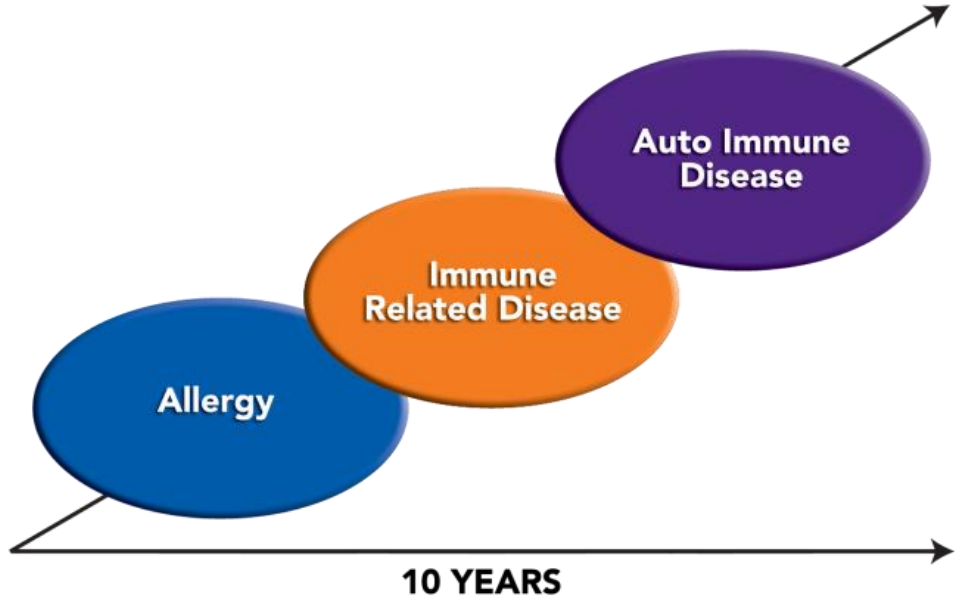
Developmental Assistance: Dunwoody Consulting

Disclosures

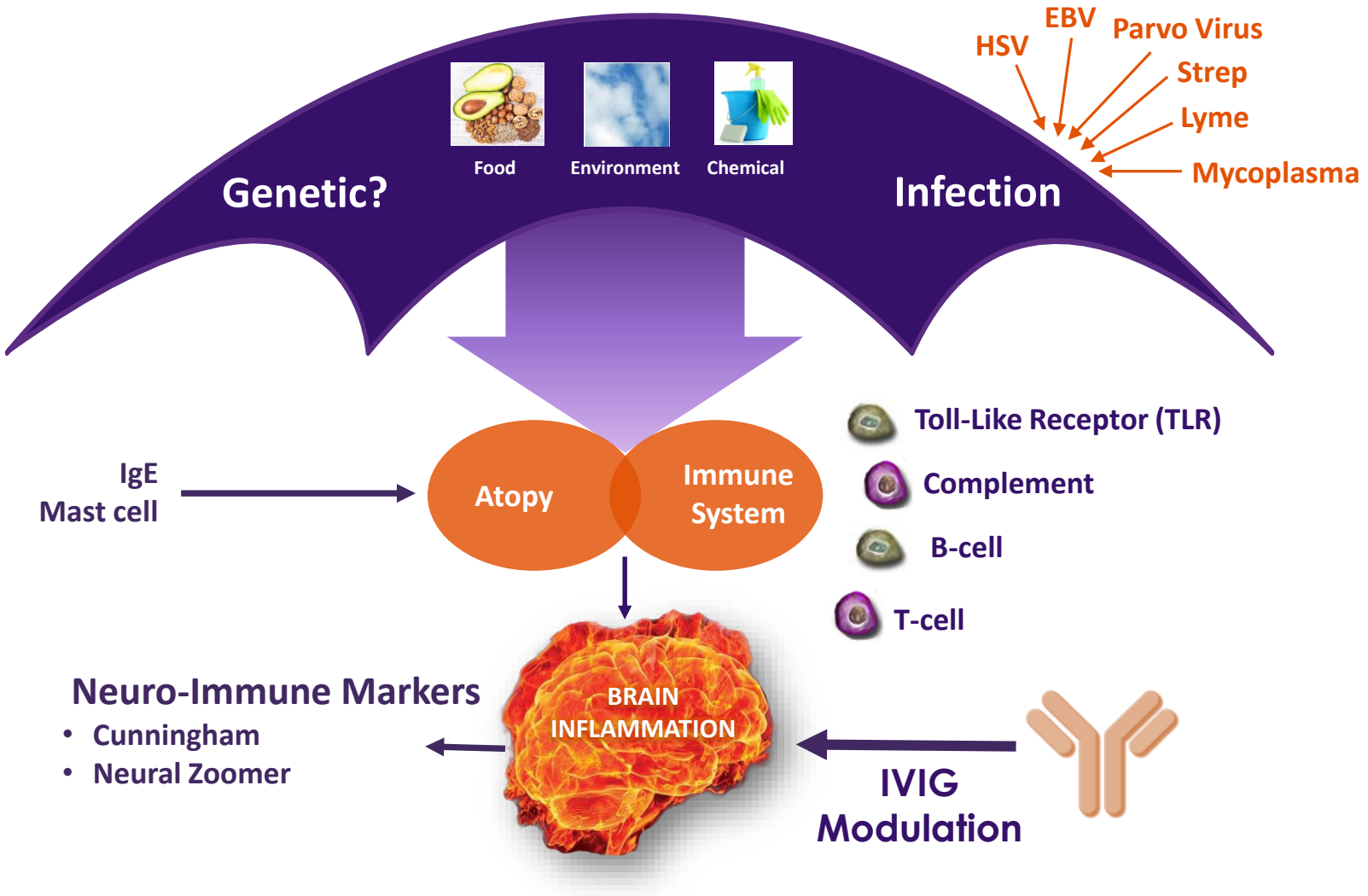
Company/Name	Honoraria/ Expenses	Funded Reearch	Royalties/ Patent	Stock Options	Ownership/ Equity Position	Employee
IMMUNOe						X
Octapharma	X	X				
Pharming Group	X	X				

Study Background

- **PANDAS: P**ediatric **A**utoimmune **N**europsychiatric **D**isorders **A**ssociated with **S**treptococcal Infections
- **PANS: P**ediatric **A**cute-onset **N**europsychiatric **S**yndrome includes all patients with this syndrome, not just those associated with streptococcal infections
- A **relationship** between a **post-infectious response** and the **sudden onset of neurologic symptoms** exists, and suggests a form of **post-infectious autoimmunity through molecular mimicry**
- As a result of our studies and observations, we've identified a number of common immune defects



PANS/PANDAS Proposed Hypothesis



Study Overview and Schematic

OBJECTIVE

Evaluate the Benefit of Octagam 5% in Subjects with PANS Syndrome

PARTICIPANTS

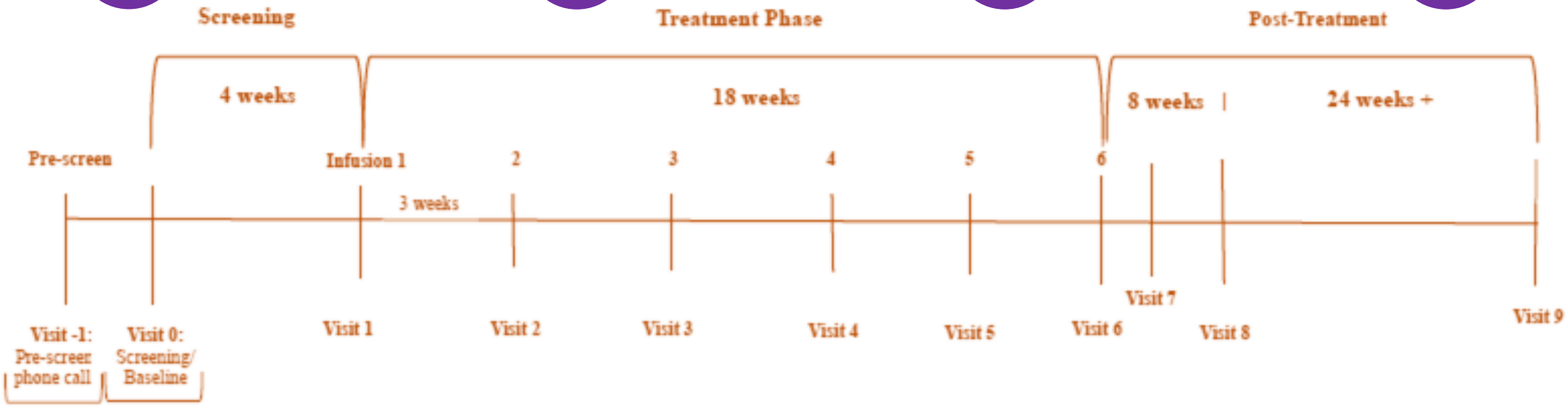
Male and Female Children Ages 4 – 16 Years with a Diagnosis of PANS

DESIGN

A Multi-site, Open-Label, Pilot Study

STUDY DRUG

Octagam 5% (1g/kg Body Weight Every 21±3 Days/6 Infusions)



Study Efficacy Endpoints

Primary Endpoints:

- Changes in Psychological Evaluation Scores from Baseline – Visits 7/8/9
  - Pediatric Acute Neuropsychiatric Symptom Scale Phone Interview Scores
  - Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS)
  - Yale Global Tic Severity Scale (YGTSS)
  - Anxiety Disorders Interview Schedule for DSM-IV (ADIS)
  - Clinical Global Impression (CGI)
  - Parent-Rated Symptom Survey
  - Parent and Patient artifacts (various)
- Change(s) in Functional TLR and Brain Autoimmunity

Demographics and Baseline Characteristics

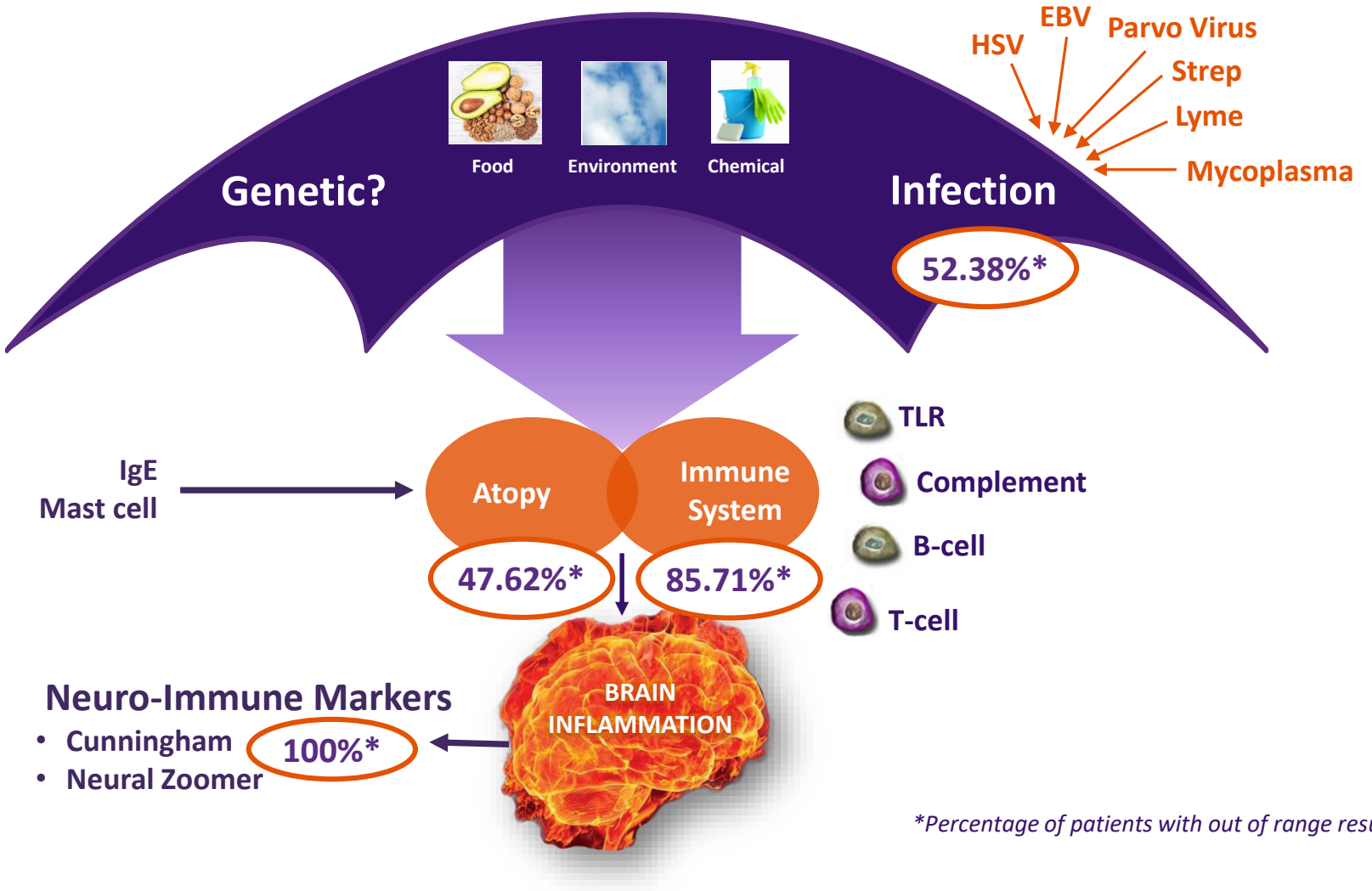
Subject Demographics

Subject Demographics	N=21
Age yrs., mean, SD	10.86 ± 2.88
Age yrs., median (range)	11 (4-16)
Gender , n (%)	
Female	8 (38)
Male	13 (62)
Race, n (%)	
White	19 (90)
Asian	1(5.0)
Asian/White	1(5.0)
Clinical Information, mean, SD	
Weight (kg)*	43.83±21.18
Pulse (bpm)	90.15±15.54
SBP	109.30±15.22
DBP	65.00±14.71
Respirations/min	16.80±2.82
Temp (F)	97.93±91.01

* Patient sample of N=20: 1 patient did not have Octagam 5% dose documented and weight measurement was missing.

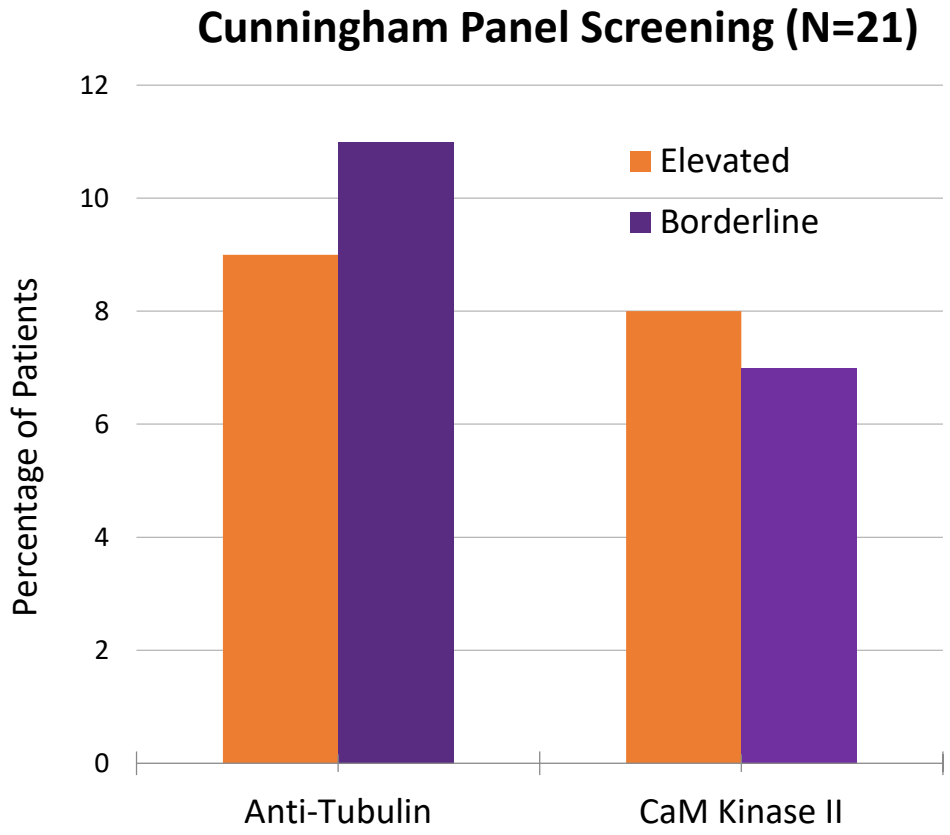
- Mean age: 10.86 years
- More males (62%) versus females
- Majority of patients were white race (90%)
- Vital signs were within normal ranges
- Octagam 5% was dosed at 1 g/kg
- Mean follow-up time from Visit 0 to Visit 8 was 186 days (±13 days)
- Late follow-up (Visit 9: 24-46+ weeks after last IVIG infusion) was implemented to gather additional data on durability of response

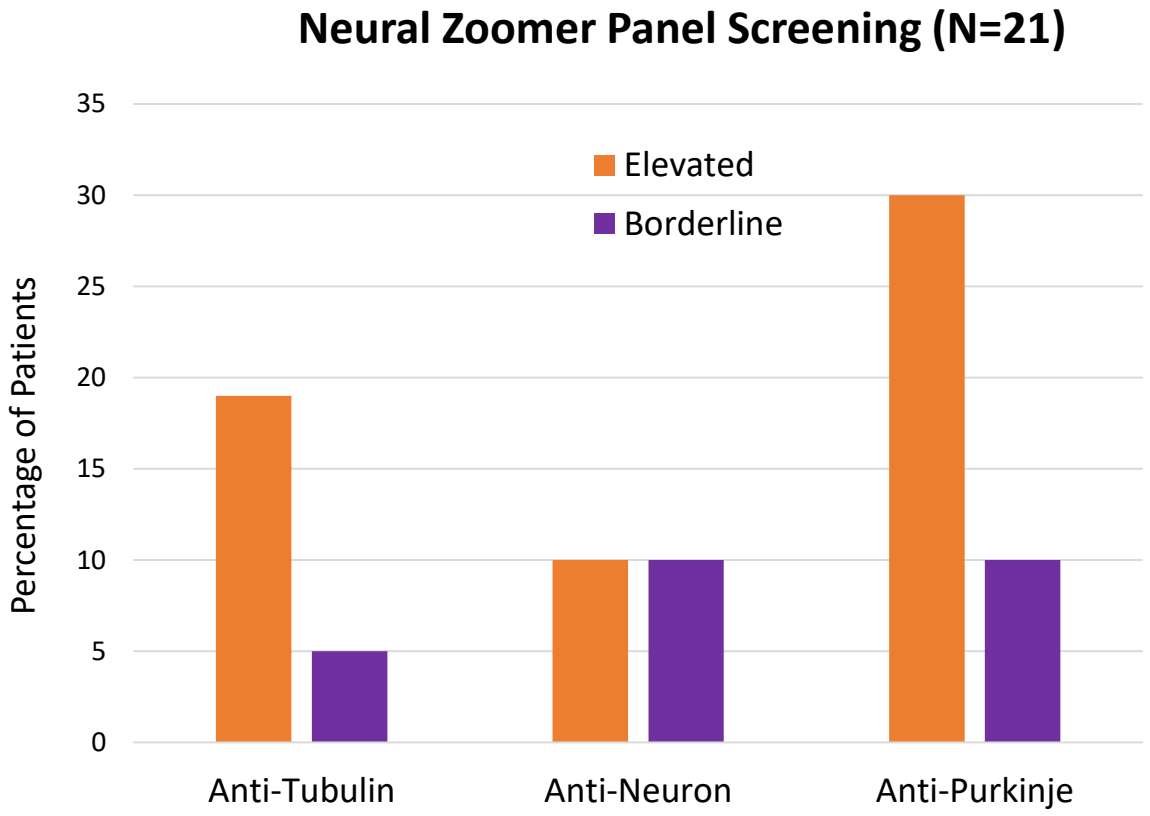
Baseline Characteristics



*Percentage of patients with out of range results

Brain Autoimmunity





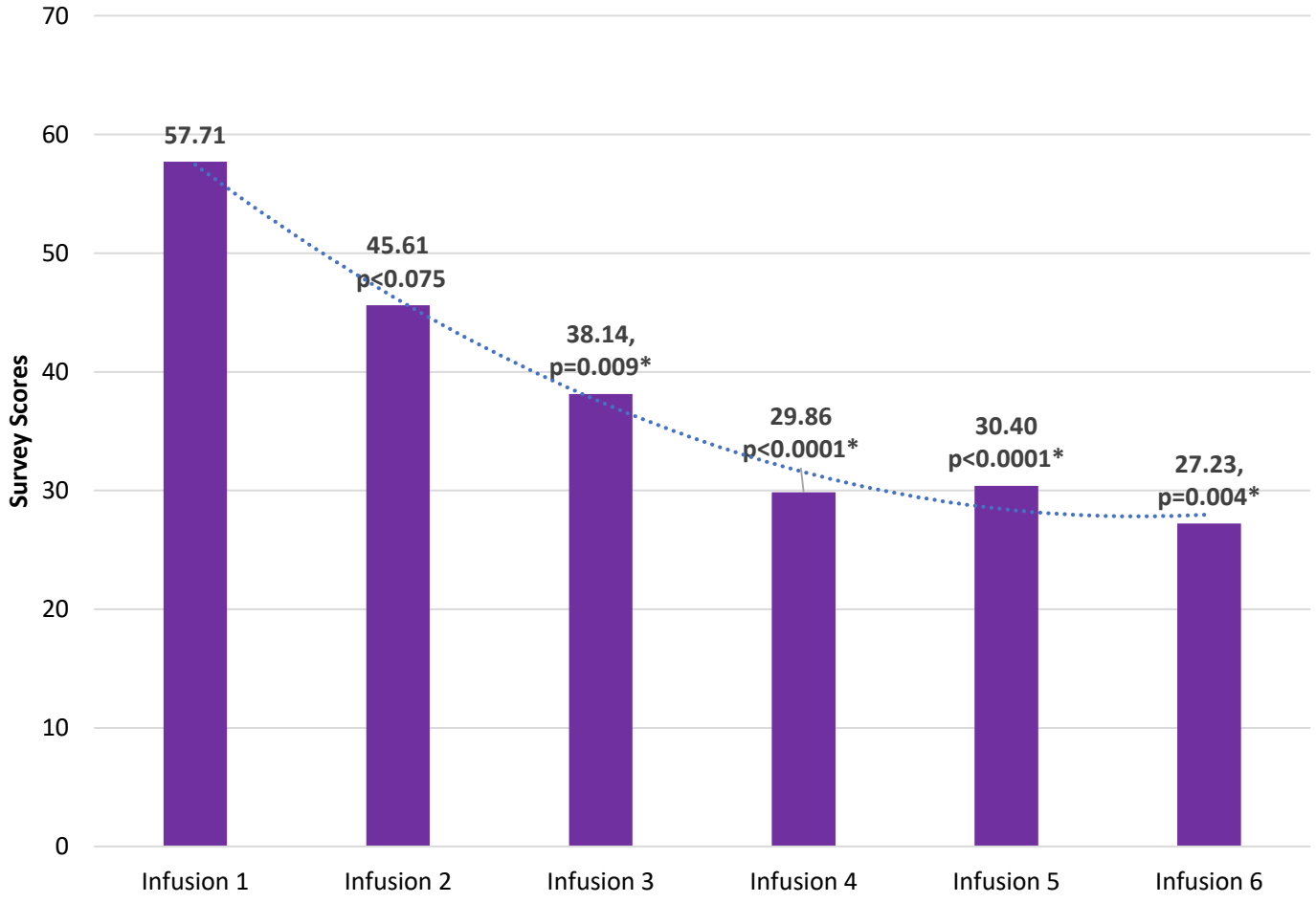
Percentage of patients with out of range Cunningham panel results: 21/21= **100%**

Percentage of patients with out of range Neural Zoomer panel results: 15/21= **71.4%**

We would like to acknowledge Moleculera Labs for their generous donation of the Cunningham Panel assessments and consultant advice.

Study Results:
Psychological (PSY) Assessments

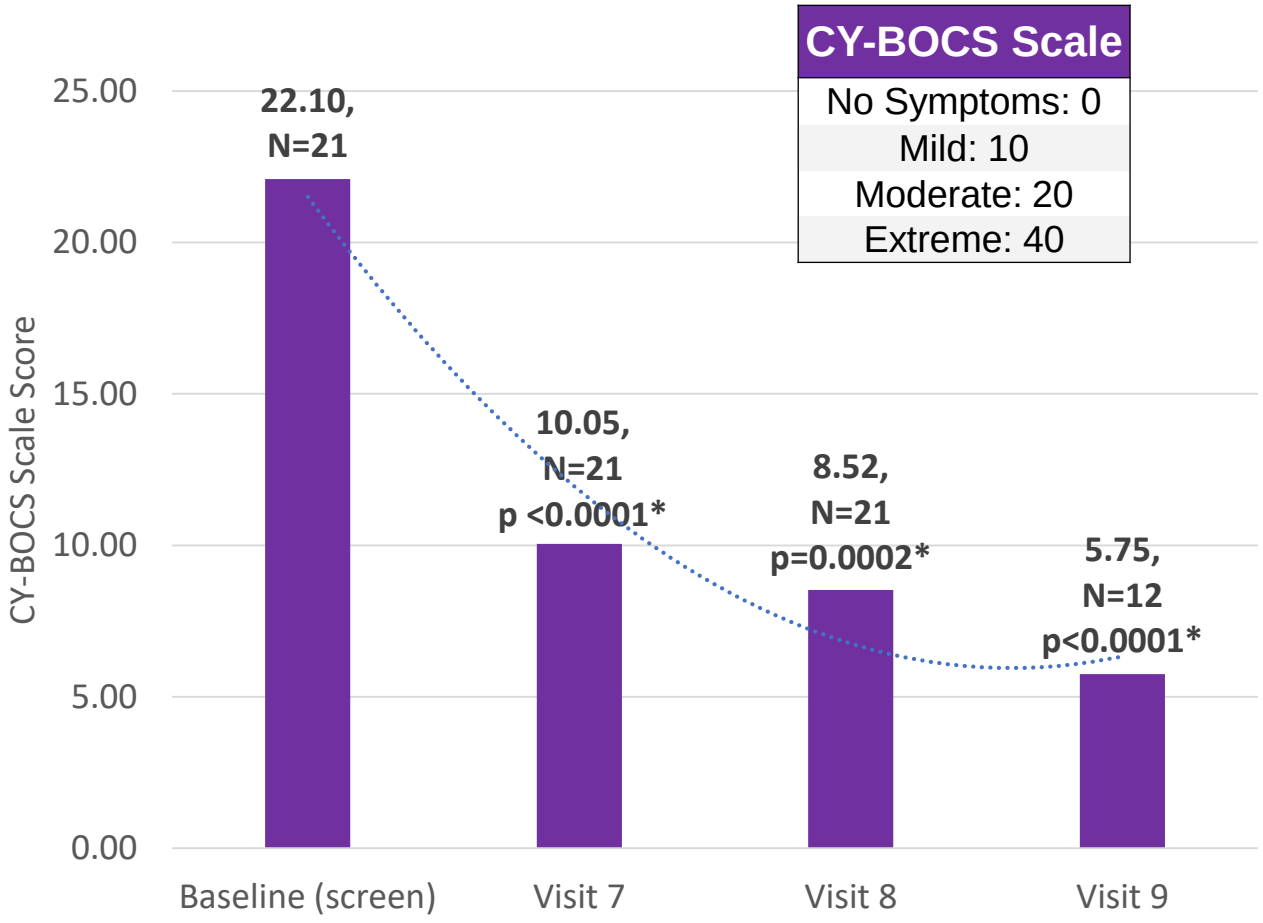
PSY Results: Parent-Rated Symptom Survey



*p value <0.05 = statistically significant

- PANS Questionnaire, 58 questions related to symptoms
- Symptoms graded from 0 (none) to 4 (extreme)
- Results indicate significant reductions in symptoms beginning at Infusion 3 through Infusion 6 (compared to treatment initiation at Infusion 1)
- Outcomes are unique and compelling – unlike other assessments that only occurred at Baseline and Visits 7/8/9, these assessments show steady improvement from Infusion 1 to Infusion 6

PSY Results: CY-BOCS



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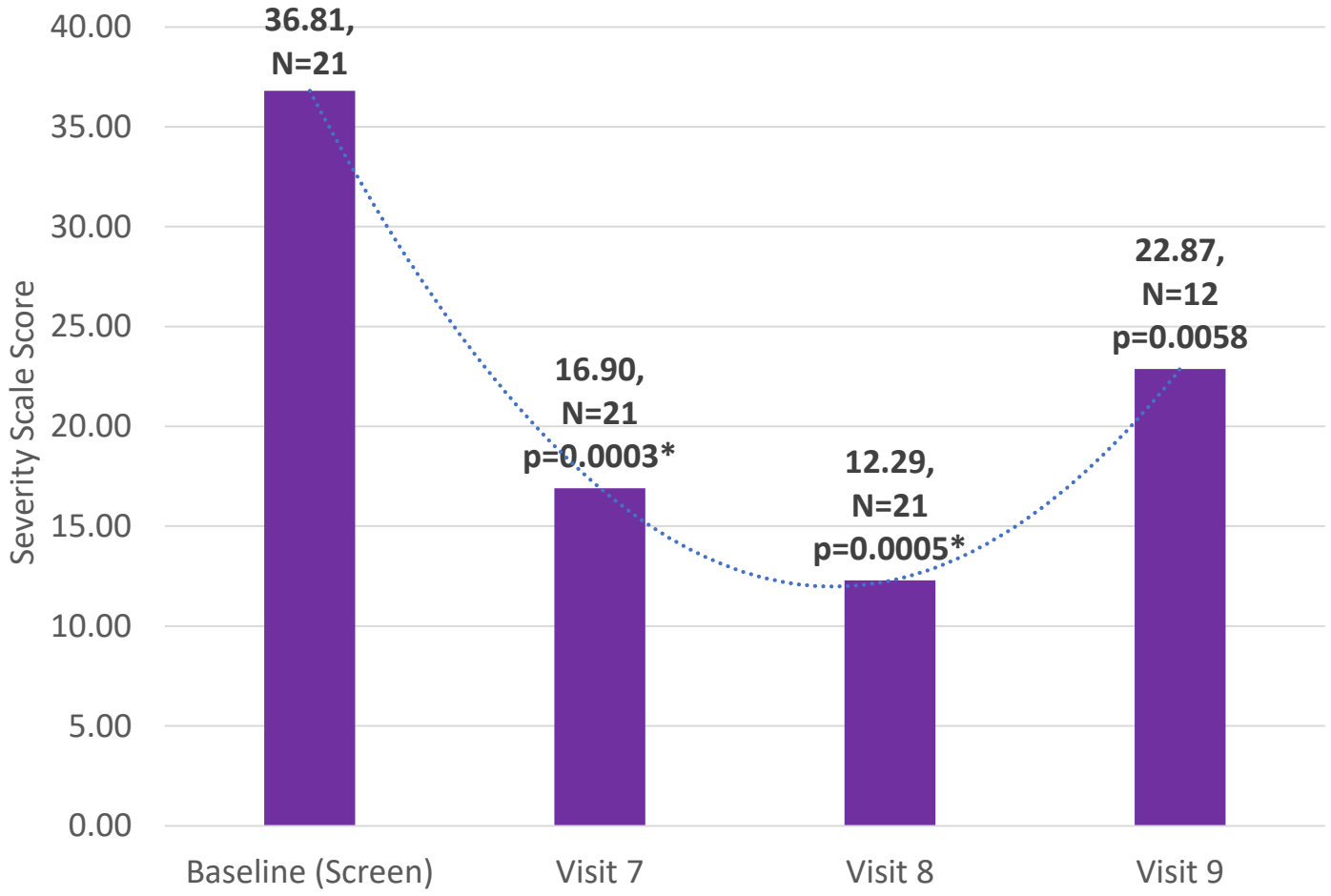
- The characteristics of obsessions and compulsions, thoughts, and behaviors
- Scaled 0 to 4, with 0 None and 4 Extreme
- Patient self-report, and, clinical judgment required; a very comprehensive measure

Study Time Point	Percentage Change	Average Change
Screen to Visit 7	-54.53%	-12.05
Screen to Visit 8	-61.42%	-13.57
Screen to Visit 9	-71.01%	-14.08
Visit 7 to Visit 8	-15.17%	-1.52
Visit 8 to Visit 9	-38.39%	-3.58

PSY Results: YGTSS



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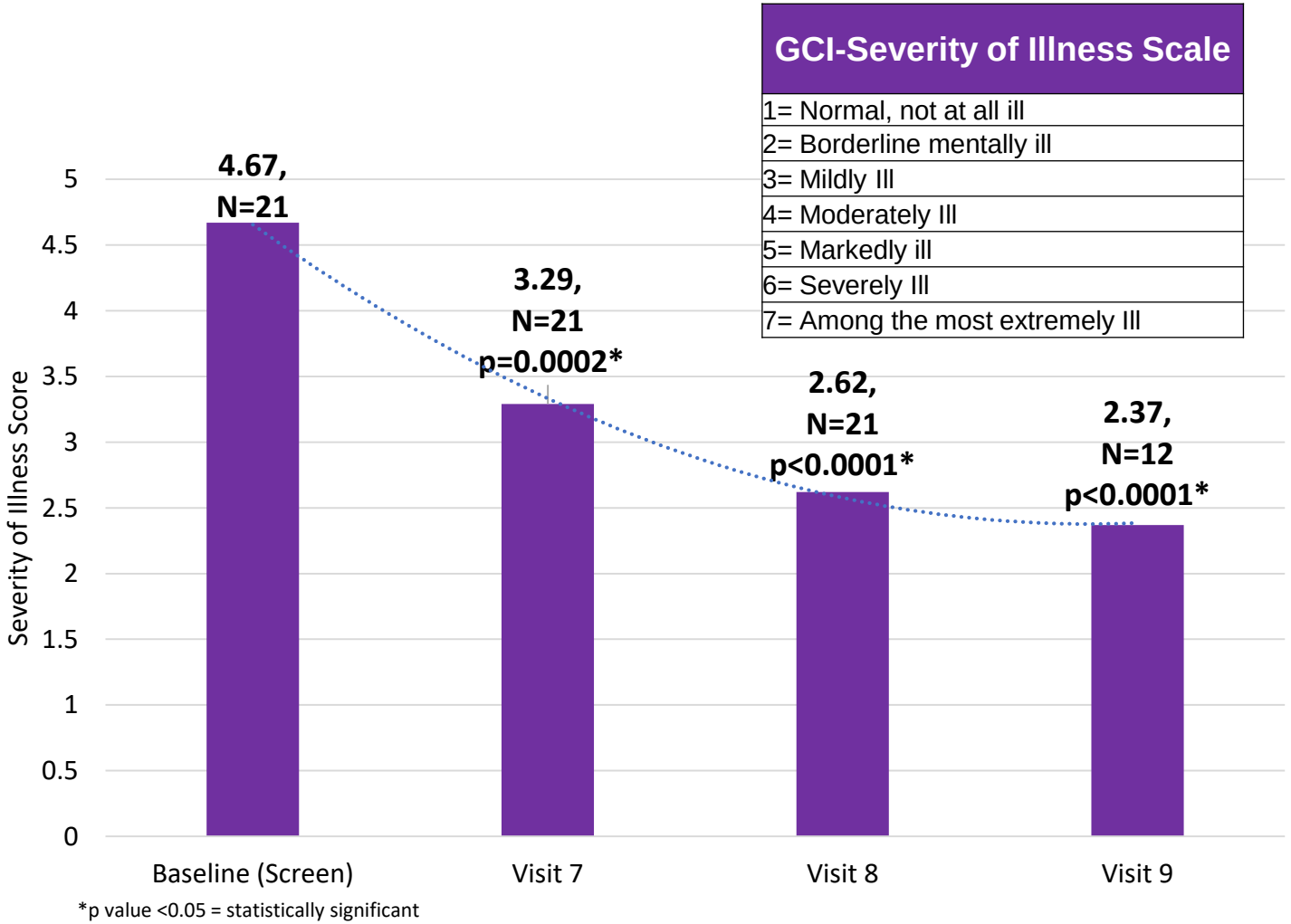
- Scale from 0 (none) to 100 (most severe)
- YGTSS scores show statistically significant decreases at Visits 7 and 8
- At Visit 9 (late follow-up), scores increased

Study Time Point	Percentage Change	Numerical Change
Screen to Visit 7	-54.1%	-19.90
Screen to Visit 8	-66.6%	-24.52
Screen to Visit 9	-44.71%	-18.50
Visit 7 to Visit 8	-27.3%	-4.62
Visit 8 to Visit 9	51.66%	7.79

PSY Results: CGI (Severity of Illness)



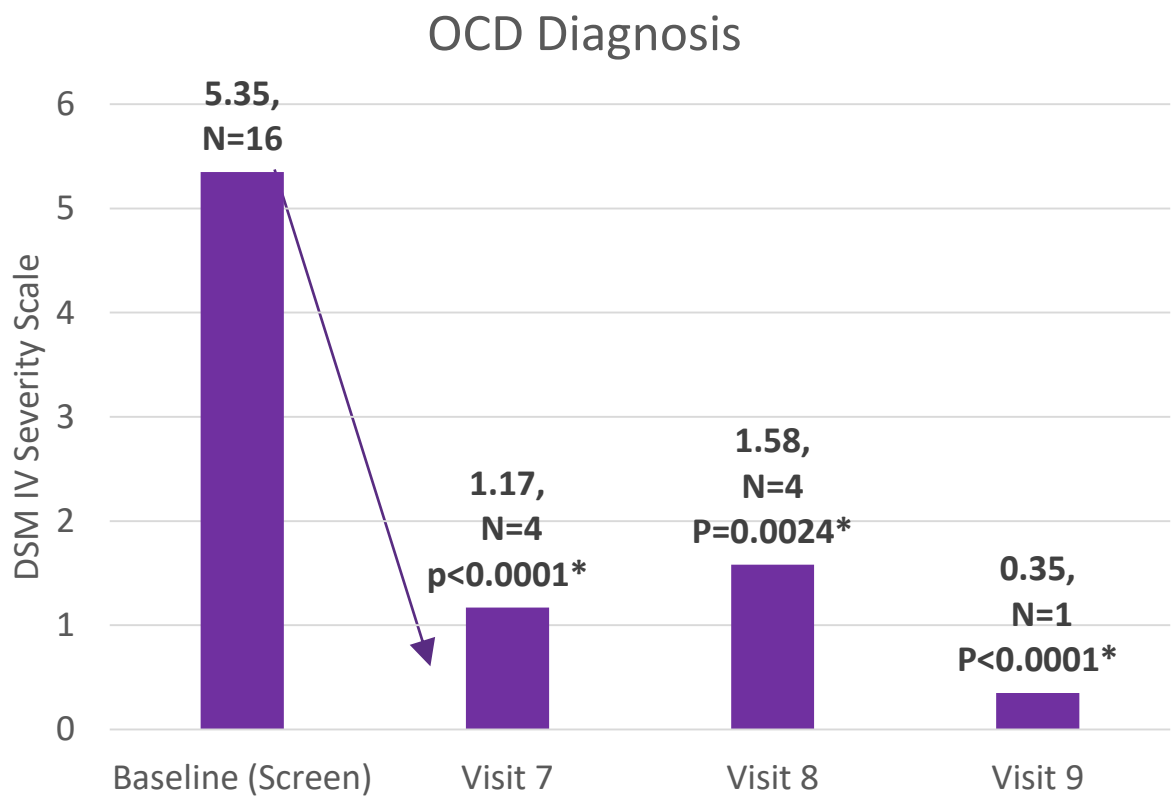
*p value <0.05 = statistically significant

GCI-Severity of Illness Scale
1= Normal, not at all ill
2= Borderline mentally ill
3= Mildly Ill
4= Moderately Ill
5= Markedly ill
6= Severely Ill
7= Among the most extremely Ill

- Scale was from 1 (normal) to 7 (extremely ill)
- The change in mean scale scores at Baseline (Screen) vs. Visits 7/8/9 were statistically significant

Study Time Point	Percentage Change	Average Change
Screen to Visit 7	-29.59%	-1.38
Screen to Visit 8	-43.88%	-2.05
Screen to Visit 9	-46.23%	-2.04
Visit 7 to Visit 8	-20.29%	-0.67
Visit 8 to Visit 9	-10.94%	-0.29

ADIS Result: Reduction in OCD

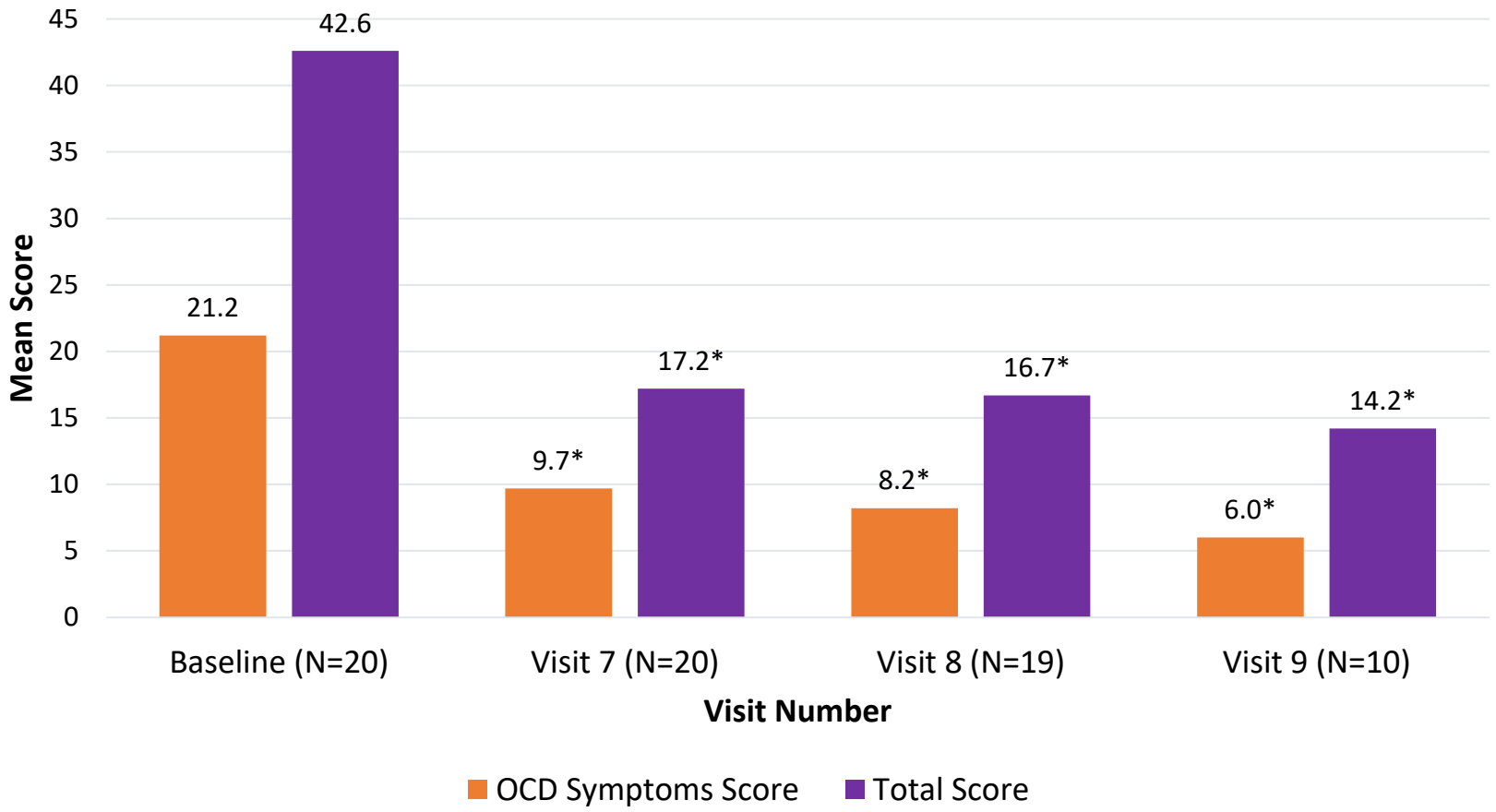


*p value <0.05 = statistically significant

- Anxiety Disorders Interview Schedule for DSM-IV, Parent Versions (ADIS) was collected at Baseline (Screen) and Visits 7/8/9 from parents
- This data displays the subset of patients with a diagnosis for OCD at Baseline (16 of 21)
- At Visit 7, only 4 patients (of the original 16) had a diagnosis of OCD
- At Visit 9, only 1 patient out of 12 (those with data at late follow-up) had a diagnosis of OCD

PSY Results: Phone Screen

- OCD and other neuropsychiatric symptoms significantly decreased from Baseline to Visits 7/8/9 (p<000.1)



*p value <0.05 = statistically significant

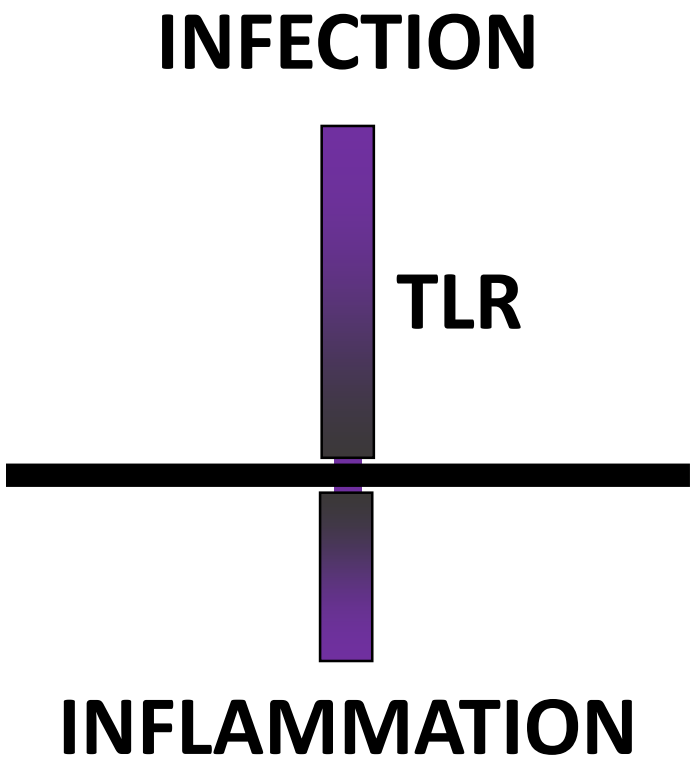
Study Results: Biomarkers

Biomarkers: TLR Functional

Statistical Overview
Mean Pre-Treatment Levels: 131.07
Mean Post-Treatment Levels: 313.49
p Value: < 0.0001**
Mean Increase in TLR Levels: 182.43

**Statistically significant (paired t test of pre/post mean values)

Toll-Like Receptors



Study Results: Drawing Sample

PSY Drawing Sample (Patient HJ, M/12)

Pre-Treatment

Draw self, draw self and others

Post-Treatment

Draw self, draw self and others

Conclusions

- In PANS patients, all psychological endpoints studied exhibited statistically significant decreases following 6 cycles (infusions) of IVIG

- PANS is an autoimmune disease
  - Innate immunity and the complement system may play a role in the pathogenesis of PANS

- Patients with PANS can benefit from a 6-cycle course of IVIG
  - Provisional late data demonstrate durability of the positive impact of IVIG treatment